```
 s libra? or combinat?
         63768 LIBRA?
        405601 COMBINAT?
L1      461799 LIBRA? OR COMBINAT?

=> s l1 and (bias?(5w)random)
         57797 BIAS?
        106333 RANDOM
           176 BIAS?(5W)RANDOM
L2           9 L1 AND (BIAS?(5W)RANDOM)

=> d l2 1-9 ab au so py ti

L2   ANSWER 1 OF 9  CA  COPYRIGHT 2002 ACS
AB   The invention relates four methods of removing mRNA 3'-untranslated
     regions (3' UTR) to optimize the formation of covalent mRNA-protein
     conjugates which may be used for in vitro selection and direct isolation
     of desired protein.  The stable covalent linkage between mRNA and the
     peptide or protein that it encodes can be generated through in vitro
     translation of synthetic mRNAs by ligating mRNA lacking 3' UTR to a DNA
     linker with a puromycin moiety (as peptide acceptor).  The first method
to
     remove 3' UTR is at the DNA level by treating the cDNA library
     with exonuclease III and Mung bean nuclease (or S1 nuclease) by adjusting
     the incubation time.  The second method is for mRNA either directly by
     linking mRNA with a linker with type IIS restriction site and then
     treating its RT-PCR products by type IIS restriction enzyme which cuts
     upstream of its site and remove stop codon as well. in the in vitro
     translation system depleted of translation releasing factor (RF) in which
     translation is paused at the stop codon.  Alternatively through in vitro
     translation system depleted of translation releasing factor (RF) in which
     translation is paused at the stop codon, the oligo(dT) primer is used for
     reverse transcription of cDNA up to the stop codon and the RNaseH is
added
     to remove the RNA-DNA duplex and release mRNA lacking 3' UTR.  The third
     method is biased random priming to make cDNA
     library by using a mixture of primers containing complementary sequence
     to a stop codon flanked by type IIS restriction sites on the 3' side and
     more random sequence at the 5' end.  The fourth method is the random
     priming approach to make first strand cDNA with the primers containing
FLAG
     epitope coding sequence at the 5' end and 9 random sequence at the 3' end
     and no stop codon in three open rading frames and to make second strand
     cDNA using primers containing an ATG codon and ribosome binding site and
T7
     RNA polymerase binding site at the 5' end and 9 random nucleotide at the
     3' end.  The final double-stranded DNA are amplified by primers with
these
     fixed sequence which is then used to transcribe mRNA with no 3' UTR.  The
     third and fourth approaches are tested with human cytochrome oxidase IV
     subunit A mRNA and polyA+ RNA from human bone marrow and HL60 resp.
IN   Hammond, Philip W.; Lipovsek, Dasa
SO   PCT Int. Appl., 52 pp.
     CODEN: PIXXD2
PY   2000
     2000
     2001
     2001
     2002
TI   Methods of producing mRNA-protein conjugates and optimizing their
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formation by removing mRNA 3'-untranslated regions

L2 ANSWER 2 OF 9 CA COPYRIGHT 2002 ACS
AB The relative spatial positioning of chromosomes 7, 8, 16, X and Y was examined in nuclei of quiescent (noncycling) diploid and triploid human fibroblasts using fluorescence in situ hybridization (FISH) with chromosome-specific DNA probes and digital imaging. In quiescent diploid cells, interhomolog distances and chromosome homolog position maps revealed a nonrandom, preferential topol. for chromosomes 7, 8 and 16, whereas chromosome X approximated a more random distribution. Variations in the orientation of nuclei on the culture substratum tended to hinder detection of an ordered chromosome topol. at interphase by **biasing** homolog position maps towards **random** distributions. Using two chromosome X homologs as reference points in triploid cells (karyotype = 69, XXY), the intranuclear location of chromosome Y was found to be predictable within remarkably narrow spatial limits. Dual-FISH with various **combinations** of chromosome-specific DNA probes and contrasting fluorochromes was used to identify adjacent chromosomes in mitotic rosettes and test whether they are similarly positioned in interphase nuclei. From among the **combinations** tested, chromosomes 8 and 11 were found to be closely apposed in most mitotic rosettes and interphase nuclei. Overall, results suggest the existence of an ordered interphase chromosome topol. in quiescent human cells in which at least some chromosome homologs exhibit a preferred relative intranuclear location that may correspond to the observed spatial order of chromosomes in rosettes of mitotic cells.
AU Nagele, Robert G.; Freeman, Theresa; McMorrow, Lydia; Thomson, Zabrina; Kitson-Wind, Kelly; Lee, Hsin-Yi
SO Journal of Cell Science (1999), 112(4), 525-535
CODEN: JNCSAI; ISSN: 0021-9533
PY 1999
TI Chromosomes exhibit preferential positioning in nuclei of quiescent human cells

L2 ANSWER 3 OF 9 CA COPYRIGHT 2002 ACS
AB The purpose of the present study was to investigate the therapeutic effectiveness of interleukin-2 (IL-2) and interferon (IFN), either alone or in **combination**, in comparable groups of patients affected by advanced renal cell carcinoma (RCC). In order to limit selection **biases**, treatment was allocated on a **random** basis. Patients randomized to IL-2 alone were scheduled to receive eight rIL-2 24-h i.v. infusion cycles, days 1 to 4, at a daily dose of 18 + 106 IU/m2 for a total of 25 wk. Patients randomized to IFN alone were scheduled to receive rIFN-α at a daily dose of 6 + 106 IU/m2, days 1,3 and 5, every week for a total of 52 wk. Patients randomized to the **combination** of IFN and IL-2 were given the same drugs at the same daily doses for a total of 24 wk. Drug dose was modified according to toxicity. Twenty-three percent (95% Cl: ± 17.5) of patients treated with IL-2 alone showed an objective response to treatment (9% CR). The corresponding figures in patients treated with IFN alone or IFN plus IL-2 were 9% (95% Cl: ± 11.9) and 9% (95% Cl: ± 11.9), resp. Complete responses were observed only in patients treated with IL-2. The median duration of response in the IL-2 arm was 18 mo (range, 9.5-24). The duration of the two responses achieved by IFN alone was seven and nine months, resp. The corresponding figures in the two patients responding to the **combination** of IFN with IL-2 were 19 and 27 mo, resp. Total

IL-2 dose appeared to be a major predictor of response. Only a minority of patients experienced grade 3-4 toxicity, the incidence being higher in those treated with IL-2 or IL-2 plus IFN. Neither IFN nor IL-2 or the **combination** of the two appear to be very active in patients with advanced RCC, even when trial entry was restricted to patients with relatively indolent disease. This stresses the need for the development of new approaches.

AU Boccardo, Francesco; Rubagotti, Alessandra; Canobbio, Luciano; Galligioni, Enzo; Sorio, Roberto; Lucenti, Antonio; Cognetti, Francesco; Ruggeri, Enrico; Landonio, Giuseppe; Baiocchi, Claudia; Besana, Carlo; Citterio, Giovanni; De Rosa, Marisa; Calabresi, Federico

SO Tumori (1998), 84(5), 534-539
CODEN: TUMOAB; ISSN: 0300-8916

PY 1998

TI Interleukin-2, interferon-α and interleukin-2 plus interferon-α in renal cell carcinoma. A randomized phase II trial

L2 ANSWER 4 OF 9 CA COPYRIGHT 2002 ACS

AB The phosphoenolpyruvate-dependent phosphotransferase system (PTS) plays a major role in the ability of Escherichia coli to migrate toward PTS carbohydrates. The present study establishes that chemotaxis toward PTS substrates in Bacillus subtilis is mediated by the PTS as well as by a methyl-accepting chemotaxis protein (MCP). As for E. coli, a B. subtilis ptsH null mutant is severely deficient in chemotaxis toward most PTS carbohydrates. Tethering anal. revealed that this mutant does respond normally to the stepwise addition of a PTS substrate (pos. stimulus) but fails to respond normally to the stepwise removal of such a substrate (neg. stimulus). An mcpC null mutant showed no response to the stepwise addition or removal of D-glucose or D-mannitol, both of which are PTS substrates. Therefore, in contrast to E. coli PTS carbohydrate chemotaxis, B. subtilis PTS carbohydrate chemotaxis is mediated by both MCPs and the PTS; the response to pos. stimulus is primarily McpC mediated, while the duration or magnitude of the response to neg. PTS carbohydrate stimulus is greatly influenced by components of the PTS and McpC. In the case of the PTS substrate D-glucose, the response to neg. stimulus is also partially mediated by McpA. Finally, we show that B. subtilis EnzymeI-P has the ability to inhibit B. subtilis CheA autophosphorylation in vitro. We hypothesize that chemotaxis in the spatial gradient of the capillary assay may result from a **combination** of a transient increase in the intracellular concentration of EnzymeI-P and a decrease in the concentration of carbohydrate-associated McpC as the cell moves down the carbohydrate concentration gradient. Both events appear to contribute to inhibition of CheA activity that increases the tendency of the bacteria to tumble. In the case of D-glucose, a decrease in D-glucose-associated McpA may also contribute to the inhibition of CheA. This **bias** on the otherwise **random** walk allows net migration, or chemotaxis, to occur.

AU Garrity, Liam F.; Schiel, Stacey L.; Merrill, Ronald; Reizer, Jonathan; Saier, Milton H., Jr.; Ordal, George W.

SO Journal of Bacteriology (1998), 180(17), 4475-4480
CODEN: JOBAAY; ISSN: 0021-9193

PY 1998

TI Unique regulation of carbohydrate chemotaxis in Bacillus subtilis by the phosphoenolpyruvate-dependent phosphotransferase system and the methyl-accepting chemotaxis protein McpC

L2 ANSWER 5 OF 9 CA COPYRIGHT 2002 ACS

AB A computational framework is presented for heuristic study of the performance of different algorithms and sampling frequencies for estimating river mass loads. The approach adopted is to generate a time series of synthetic concentration, from a time series of observed streamflow, on the basis of available information on the covariation of flow and concentration for the determinand and site of interest. A reference mass load for the whole, or any part, of the time series is calculated from the flow and synthetic concentration time series. **Combinations** of different estimation algorithms and (periodic) sampling intervals can be applied and the resultant mass load ests. compared with the reference value. For a chosen estimation algorithm, the distribution of mass load ests. derived from replicated samples leads to measures of accuracy (**bias**) and precision (**random** error). A qual. comparison of the performance of 2 mass load estimation algorithms, specified by the Paris Commission for monitoring fluvial inputs to the North Sea, is presented using the hydrol. regime of a 20-km2 catchment in southwest England and 2 general cases of hysteretic concentration behavior: concentration increases with flow and concentration decreases with flow. In each case, a better estimate of river mass load is obtained when the variation in flow between concentration samples is taken into account.
AU Littlewood, I.G.
SO Environ. Int. (1995), 21(2), 211-20
CODEN: ENVIDV; ISSN: 0160-4120
PY 1995
TI Hydrological regimes, sampling strategies, and assessment of errors in mass load estimates for United Kingdom rivers

L2 ANSWER 6 OF 9 CA COPYRIGHT 2002 ACS
AB Cassette mutagenesis is a method of protein engineering which generates a wide diversity of genetic variants that can be subjected to either selection or screening. As long as the target sequence to be modified is kept short (corresponding to four to six amino acids), complete **combinatorial libraries** can be produced. A major problem arises when longer peptides are to be engineered for desired functions. In such situations the production of a limited collection of variants can be helpful; thus, **biased random** mutagenesis and doping schemes have been reported previously. Here the authors describe a computer algorithm that enables the determination of the degree of phosphoramidite contamination of nucleotide precursor reservoirs. Through simulation of biol. translation, the algorithm allows the prediction of the effect of contamination levels on the number of mutations to occur for any given peptide sequence. In this study the cholinergic binding site was used as a model sequence (22 amino acids). Considerations, based on the computer program, are discussed regarding the efficient design of phage-display **combinatorial libraries**.
AU Ophir, Ron; Gershoni, Jonathan M.
SO Protein Eng. (1995), 8(2), 143-6

CODEN: PRENE9; ISSN: 0269-2139
PY 1995
TI **Biased random** mutagenesis of peptides: determination of mutation frequency by computer simulation

L2 ANSWER 7 OF 9 CA COPYRIGHT 2002 ACS
AB A method of synthesizing isolated, soluble peptides having constrained secondary structure in solution is described herein. The peptides are encoded by expressible oligonucleotides having a desirable **bias** of **random** codon sequences. Individual nucleotides instead of triplets are used to prepare the oligonucleotides. A non-degenerate subset of all triplets is synthesized at any one position, thereby alleviating codon redundancy. Using this method, one can randomize at certain positions and select for specific codons at others, e.g., codons specifying amino acids which can form an intrachain covalent bond. In a preferred method, two precursor oligonucleotides with biased sequences are prepared such that one precursor is the sense sequence for the amino terminus and the other precursor is the antisense sequence for the carboxy terminus and the sequences are partially complementary. The precursors and oligonucleotide produced from the two precursors may be cloned in M13 fused to a gene VIII sequence. Eight soluble, conformationally constrained peptides with high affinity for anti-tetanus toxin antibody were prepared by this method.
IN Huse, William D.
SO PCT Int. Appl., 150 pp.
CODEN: PIXXD2
PY 1994
1994
1995
1996
1998
TI Soluble peptides having constrained, secondary conformation in solution and method of making same

L2 ANSWER 8 OF 9 CA COPYRIGHT 2002 ACS
AB **Libraries** of random oligonucleotides are prepared in which the amino acid bias resulting from the redundancy of the genetic code is avoided. These sequences are expressed in constructs in which the resulting peptides are presented on the surface of the host. Random triplets are synthesized using a mixture of all four nucleotides for the first two positions and a mixture of guanine and thymine for the third position. Randomization can be modulated by changing the ratios of oligonucleotides in each reaction. These are then assembled into random oligomers. M13-based expression vectors for these oligonucleotides are described.
IN Huse, William D.
SO PCT Int. Appl., 141 pp.
CODEN: PIXXD2
PY 1992
1992
1992
1995
1993
1994
2001

1998
2001
TI Surface expression **libraries** of randomized peptides

L2 ANSWER 9 OF 9 CA COPYRIGHT 2002 ACS
AB An apparatus was constructed to measure quant. the chemotactic response of
bacterial populations, using a linear d. gradient of glycerol to stabilize
a solution in an observation cell. At low bacterial concentration the right angle
of scattered light was proportional to concentration The apparatus was flexible,
allowing a wide variety of gradients, of which the following were the most
useful: a steep gradient between two concns. over a short distance; a
linear gradient to measure reponse to absolute differences in concentration; and an
exponential gradient to measure responses to ratios of concns. The most
useful theoretical **combinations** seemed to be a form of bacterial
popula-tion superposed on one of these three attractant gradients. The
bacteria appeared to move in all directions but with a preference for
movement in the direction of the gradient, suggest-ing a **biased**
random walk (J. B. Armstrong, J. Adler, and M. A. Dahl, 1967; and
H. J. Vogel and D. M. Bonner, 1956) as an explanation for chemotaxis.
AU Dahlquist, F. W.; Lovely, P.; Koshland, D. E., Jr.
SO Nature (London), New Biol. (1972), 236(65), 120-3
CODEN: NNBYA7
PY 1972
TI Quantitative analysis of bacterial migration in chemotaxis